

In the Claims

Please cancel claims ~~1, 2, 9-12, 16, 17, 71, 73-75, 77, 182-184, 191, and 193-204,~~
without prejudice.

Please rewrite the following claims as indicated below. A marked-up version of
the rewritten claims is appended hereto illustrating the changes.

94 3. A method as in claim 60, wherein the auxiliary signaling entity comprises a dye,
pigment, electroactive molecule, chemiluminescent moiety, electrochemiluminescent
moiety, fluorescent moiety, up-regulating phosphor, or enzyme-linked signaling moiety
including horse radish peroxidase and alkaline phosphatase.

95 6. A method as in claim 60, comprising providing a plurality of colloid particles and
the non-colloidal structure in proximity such that the plurality of colloid particles fasten
to the non-colloidal structure, and determining fastening of the plurality of particles to the
non-colloidal structure.

13. A method as in claim 60, comprising providing the agent linked to the non-
colloidal structure, the binding partner linked to the particle, and providing the colloid
particle and the non-colloidal structure in proximity such that the agent and the binding
partner bind to each other.

96 14. A method as in claim 13, comprising providing the colloid particle and the non-
colloidal structure in proximity such that the agent and the binding partner biologically
bind to each other.

15. A method as in claim 60, wherein the biological or chemical agent is a drug
candidate, and the binding partner is a target of the drug candidate.

18. A method as in claim 60, wherein the biological or chemical agent is a nucleic acid sequence.

19. A method as in claim 60, wherein the biological or chemical agent is a peptide, and the binding partner is a binding partner of the peptide.

20. A method as in claim 60, wherein the biological or chemical agent is a protein, and the binding partner is a binding partner of the protein.

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21. A method as in claim 60, wherein the colloid particle carries an immobilized ligand, and the non-colloidal structure carries a binding partner to the ligand, and wherein the step of providing the colloidal particle and the non-colloidal structure in proximity is performed in the presence of a candidate drug for interruption of binding of the ligand to the binding partner.

22. A method as in claim 60, further comprising providing a plurality of magnetic beads, a plurality of biological or chemical agents linked to or adapted for linkage to the beads, a plurality of colloid particles, and a plurality of binding partners of the biological or chemical agents linked to or adapted for linkage to the particles, wherein at least some of the agents and the binding partners are suspected of having the ability to bind to each other, the method comprising exposing at least some of the magnetic beads to at least some of the colloid particles, and determining immobilization of the colloid particles on the magnetic beads.

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26. A method as in claim 60, comprising determining immobilization of the particle on the non-colloidal structure by determining a change in spectrum of absorbed or transmitted electromagnetic radiation interacting with the particle.

27. A method as in claim 60, comprising determining immobilization of the particles on the non-colloidal structure by visual inspection.

29. A method as in claim 60, wherein at least one of the agent or binding partner is linked to or adapted for linkage to the non-colloidal structure or particle, respectively, via an affinity tag/binding partner linkage.

30. A method as in claim 60, wherein at least one of the agent or binding partner is linked to or adapted for linkage to the non-colloidal structure or particle, respectively, via a metal binding tag/metal/chelate linkage.

32. A method as in claim 60, wherein the binding partner is linked to or adapted for linkage to the particle via the self-assembled monolayer and/or the agent is linked to or adapted for linkage to the magnetic bead via a self-assembled monolayer of a plurality of molecules thereon.

33. A method as in claim 60, wherein at least one of the agent or binding partner is linked to or adapted for linkage to the bead or particle, respectively, via complementary nucleic acid sequence pairs.

34. A method as in claim 60, wherein the binding partner is adapted for linkage to the particle via a glutathione/glutathione-s-transferase ligand interaction.

35. A method as in claim 60, comprising:
providing at least a first and a second magnetic beads and at least a first and a second agent linked to the first and second beads, respectively;
providing a plurality of colloid particles each carrying immobilized thereto a suspected binding partner of the first and/or second agent;
exposing the beads to the particles; and

differentiating linkage of the particles to the first bead versus the second bead.

36. A method as in claim 35, wherein the first and second agents linked to the first and second magnetic beads are suspected of biological or chemical interaction with the binding partner, and the differentiating step comprises differentiating biological interaction between the first agent and the binding partner versus the second agent and the binding partner.

37. A method as in claim 60, comprising:

providing a plurality of magnetic beads each carrying the agent immobilized thereto;

providing a first set and a second set of colloid particles, the first set each carrying immobilized thereto a first suspected binding partner of the agent and the second set each carrying immobilized thereto a second suspected binding partner of the agent;

exposing at least a first of the beads to the first set of particles and at least a second of the beads to the second set of particles;

differentiating linkage of the first set of particles to the first bead versus the second set of particles to the bead.

38. A method as in claim 37, wherein the first and second suspected binding partners are suspected of biological or chemical interaction with the agent, and the differentiating step comprises differentiating biological interaction between the agent and the first suspected binding partner versus the agent and the second suspected binding partner.

60. A method for determining immobilization of a colloid particle relative to a non-colloidal structure comprising:

providing a biological or chemical agent linked to or adapted for linkage to a non-colloidal structure, and a binding partner of the biological or chemical agent linked to or

adapted for linkage to a colloidal particle having a self-assembled monolayer of a plurality of molecules thereon;

providing the colloid particle and the non-colloidal structure in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other via the agent and the binding partner; and

determining immobilization of the colloid particle relative to the non-colloidal structure; wherein

the non-colloidal structure is a magnetic bead and the colloid particle comprises an auxiliary signaling entity.

72. A method for determining immobilization of a colloid particle relative to a non-colloidal structure comprising:

providing a colloid particle and a non-colloidal structure in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other;

exposing the colloid particle and the non-colloidal structure to an entity adapted for linkage both to the colloid particle and to the non-colloidal structure in the presence both of an enzyme having the ability to cleave the entity and a candidate drug for moderation of activity of the enzyme; and

determining immobilization of the colloid particle relative to the non-colloidal structure; wherein

the non-colloidal structure is a magnetic bead and the colloid particle carries an immobilized electroactive species, and wherein the determining step comprises

magnetically drawing the bead into proximity with an electrode, and determining proximity of the electroactive species to the electrode by activating the electrode thereby determining effectiveness of the drug candidate in inhibiting cleavage activity of the enzyme.

76. A method for determining immobilization of a colloid particle relative to a non-colloidal structure comprising:

providing a colloid particle and a non-colloidal structure in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other;

exposing the colloid particle and the non-colloidal structure to a substrate for an enzyme adapted for linkage to the non-colloidal structure, a molecular species linkable to the substrate via enzyme activity adapted for linkage to the particle, and an enzyme for the substrate; and

determining immobilization of the colloid particle relative to the non-colloidal structure; wherein

the non-colloidal structure is a magnetic bead and the colloid particle carries an immobilized electroactive entity, and wherein the determining step comprises

magnetically drawing the bead into proximity with an electrode, and determining proximity of the electroactive entity to the electrode by activating the electrode thereby determining effectiveness of the drug candidate in moderating activity of the enzyme.

78. A method for determining immobilization of a colloid particle relative to a non-colloidal structure comprising:

providing a colloid particle and a non-colloidal structure in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other;

exposing the colloid particle and the non-colloidal structure to a substrate for an enzyme adapted for linkage to the non-colloidal structure, a molecular species linkable to the substrate via enzyme activity adapted for linkage to the particle, and an enzyme for the substrate; and

determining immobilization of the colloid particle relative to the non-colloidal structure; wherein

the non-colloidal structure is a magnetic bead.

Q15 185. A method as in claim 60, wherein the signaling entity comprises an electroactive entity, and wherein the binding partner and the electroactive entity each form part of the self-assembled monolayer on the colloid particle.

189. A method as in claim 185, wherein the electroactive entity comprises a ferrocene derivative.

Q16 190. A method as in claim 185, wherein the binding partner is linked to a self-assembled monolayer-forming species, which comprises at least one of the plurality of molecules forming the self-assembled monolayer, via a metal binding tag/metal/chelate linkage.

Q17 192. A method as in claim 60, wherein the non-colloidal structure carries a self-assembled monolayer thereon.

Please add the following new claims.

Q18 205. A method for determining immobilization of a colloid particle relative to a non-colloidal structure comprising:

providing a biological or chemical agent linked to or adapted for linkage to a non-colloidal structure, and a binding partner of the biological or chemical agent linked to or adapted for linkage to a colloidal particle, wherein at least one of the agent and binding partner is adapted for linkage to the non-colloidal structure or particle, respectively, via an affinity tag/binding partner linkage;

providing the colloid particle and the non-colloidal structure in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other via the agent and the binding partner; and

determining immobilization of the colloid particle relative to the non-colloidal structure; wherein

the non-colloidal structure is a magnetic bead and the colloid particle comprises an auxiliary signaling entity.

206. A method for determining immobilization of a colloid particle relative to a magnetic bead comprising:

providing a colloid particle, which comprises an auxiliary signaling entity and has a self-assembled monolayer of a plurality of molecules thereon, and a magnetic bead in proximity such that, under at least one set of predetermined conditions, the colloid particle and the non-colloidal structure will become immobilized with respect to each other; and

determining immobilization of the colloid particle relative to the magnetic bead.

207. A method as in claim 205, wherein the colloid particle has a self-assembled monolayer of a plurality of molecules thereon.

208. A method as in claim 207, wherein the colloid particle has a self-assembled mixed monolayer of a plurality of molecules thereon.

209. A method as in claim 207, wherein the self-assembled monolayer is formed completely of synthetic molecules.

210. A method as in claim 207, wherein the self-assembled monolayer completely covers the colloid particle surface.

211. A method as in claim 209, wherein the self-assembled monolayer completely covers the colloid particle surface.

212. A method as in claim 207, wherein at least one molecule forming the self-assembled monolayer comprises a thiol species terminating in a binding partner of an affinity tag.

213. A method as in claim 206, wherein the colloid particle has a self-assembled mixed monolayer of a plurality of molecules thereon.

214. A method as in claim 206, wherein the self-assembled monolayer is formed completely of synthetic molecules.

215. A method as in claim 206, wherein the self-assembled monolayer completely covers the colloid particle surface.

216. A method as in claim 214, wherein the self-assembled monolayer completely covers the colloid particle surface.

217. A method as in claim 206, wherein at least one molecule forming the self-assembled monolayer comprises a thiol species terminating in a binding partner of an affinity tag.

218. A method as in claim 206, wherein the self-assembled monolayer on the colloid particle enables the colloid particle to resist non-specific adsorption without the need for treatment with a blocking protein.

219. A method as in claim 206, further comprising providing a plurality of colloid particles, each of which has a self-assembled monolayer of a plurality of molecules thereon, wherein the self-assembled monolayer is configured such that the particles can be maintained free of aggregation in a solution that is free of any detergents.